

POSITIVE ELECTRICAL VARIATION IN ISOLATED NERVE.

By W. A. JOLLY.

(Received May 15, 1912.)

(With Five Text-figures.)

The electrical changes which occur in living tissue form a valuable part of our data in the investigation of vital processes. In living nerve the difficulty of demonstrating any change of form, chemical change or evolution of heat, or distinct histological modification accompanying activity renders the study of the electrical changes especially important.

These changes in nerve are various. Some are clearly dependent on its physical properties of electrolytic conduction and polarisation, others must be ascribed to its special activities as living tissue. Wide generalisations regarding the anabolism and katabolism of all living tissues are to a considerable extent based upon the changes of opposite sign which occur in nerve.

The literature on the subject is very extensive, and many different instruments and methods of investigation have been employed.

It is no easy matter to correlate the results obtained by different observers in this branch of research and to interpret them in the light of later work.

The following contribution to the subject forms a sequel to work undertaken in the Physiological Laboratory of Edinburgh University, the results of which were communicated to the Physiological Society of England.

When a nerve isolated from the body is stimulated by the faradic current it was shown by Hering* that at the close of the stimulation an electrical variation appears which deflects a galvanometer in the same direction as the demarcation current of the nerve, that is to say, there is a positive variation.

* Beitr. z. allgem. Muskel u. Nervenphysiologie. 15 Mitt. Sitzungsber. d. Wiener Akad. Bd. 89. 3 Abt. 1884.

During stimulation the moving part of the instrument is deflected in the opposite direction to the demarcation current, and this constitutes the negative variation.

A negative variation accompanies activity of living nerve, and when the leading off electrodes are applied to a nerve dissected out from the body of a newly killed frog, one on the uninjured longitudinal surface and the other on the cross-section, the instrument is deflected under the influence of the action current developed at the electrode on the uninjured spot. The changes giving rise to action current do not, in consequence of the injury, occur at the cross-section, or only to a slight extent.

The positive after-variation was regarded by Hering and also by Head,* who later investigated the phenomenon, as occurring in the neighbourhood of the electrode upon the longitudinal surface, and was attributed to a process occurring in the nerve opposed to that process which may be termed excitation.

According to Hering's conception, stimulation of a nerve produces phasic upward and downward changes, and at the close of a period of stimulation the positive variation which occurs evidences a process of building up or assimilation, a restitution process in the nerve which follows its period of activity.

Head discussed the possibility that the occurrences giving rise to the positive change are located at the cross-section. The appearance of positive change would be presented if the cross-section of the nerve were to become more negative to the longitudinal surface than before stimulation, that is to say, if the demarcation current were increased by the tetanisation. Head came to the conclusion that it is more probable that the process is localised not at the cross-section but at the longitudinal surface, and agrees with Hering that it accompanies a process of restitution.

Waller† found that where the nerve has been preserved for several hours before stimulation, in place of the usual negative variation accompanying activity, a positive variation may be obtained. In explanation of this reversal Waller suggests several possibilities. (1) It may be due to a reversal of action (or of greater action) in the parts of the nerve at and near the two leading-off electrodes. Since the normal negative deflection is due to action predominant near the electrode on the longitudinal surface of the nerve, the positive deflection now obtained might depend upon action becoming predominant at the cross section in consequence of some accidental and progressive injury near the longitudinal lead off. (2) The positive deflection may be a phenomenon of the same order as the positive after-variation described by Hering. (3) The reversal may be due

* Pfüger's Arch. Bd. 40 S. 207, 1887.

† Phil. Trans. London, 1896.

to electrotonic changes produced in the nerve by the stimulating current. Waller took the view that the second of these possibilities is the more probable.

Since the invention by Einthoven of the string galvanometer, this instrument has been employed in the investigation of the electrical changes in nerve.

Fig. 1 shows the negative variation produced by a period of tetanisation of 30 sec., followed by the positive after-variation. The leading off non-polarisable electrodes have been placed in my experiments, one on the

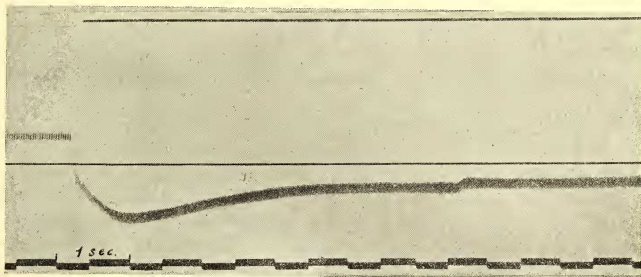


FIG. 1.

Response obtained from freshly isolated sciatic nerves of frog after tetanisation for 30 sec. Non-polarisable electrodes applied to longitudinal surface and cross-section, 1 cm. between electrodes. Resistance of preparation and electrodes = 25,000 Ohms. Upper line = signal indicating cessation of tetanisation. Zero line is marked by shadow of bristle. A control curve is given, representing the introduction into galvanometer circuit of a potential difference of 10^{-4} Volts. Lowest line = time marker indicating seconds.

The record, which reads from left to right, shows (1) the termination of an upward deflection, the negative variation or action current, upon which are superposed the individual responses to the induction shocks, (2) a downward deflection, the positive after-variation, and (3) persisting positive change.

longitudinal surface of the nerve and the other on the cross-section. The stimulating electrodes are of platinum and lie at the central end of the nerve. They are of the form recommended by Engelmann. Where localised cooling has been used the nerve between the leading-off electrodes is passed through a slit in a cardboard screen and the slit is closed by moist kaolin clay. The nerve and electrodes are enclosed in a moist chamber.

Like Waller, I have found that the electrical variation accompanying activity may be reversed, and this is so especially if the nerves have been preserved for a considerable time before experiment.

Fig. 2 gives an example of this obtained from a nerve sixteen hours after preparation.

Garten* has shown that in experiments in which the leading-off electrodes are applied to two points on the uninjured longitudinal surface the action current may present itself, when the distal electrode is cooled, as a deflection of the galvanometer which would appear to indicate relative negativity of the cooled distal electrode. The explanation offered by Garten is that the action current at the distal electrode, although probably developed with less electromotive force than at the proximal electrode, yet persists considerably longer, and therefore exercises a predominant influence upon the galvanometer.

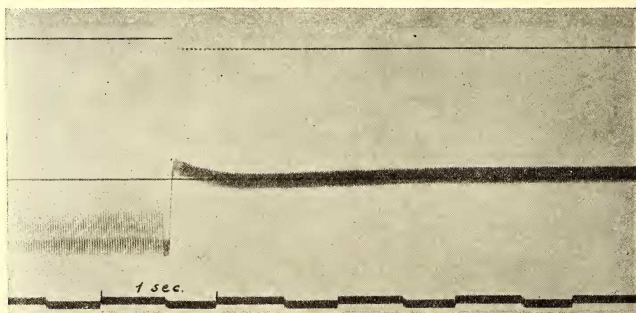


FIG. 2.

Response from nerves after preservation for 16 hours in Ringer's fluid, without fresh section. The curve shows action current as downward or positive variation.

Garten used the string galvanometer in his investigation, and the curve recorded under the conditions above-mentioned shows a deflection below the zero line during stimulation, caused by the predominant influence of the second phase of the action current, upon which the separate responses to the tetanising shocks are superposed. Garten assumes that if the two electrodes are at the same temperature the record will show merely rapid oscillations about the zero line corresponding to the diphasic action currents.

I would put forward a similar explanation for the reversal of the variation accompanying activity obtained in my experiments.

When the nerve is used immediately after removal from the body, the process of excitation is confined entirely, or almost entirely, to the uninjured

* Pflüger's Archiv. Bd. 136 S. 545, 1910.

portion of the nerve. The tissue at the cross-section is not able, owing to the injury, to develop perceptibly the condition of excitation. The result is that the action current appears as a large upward deflection—the negative variation—with the separate deflections superposed.

After preservation for some hours in Ringer's fluid, the effects of the injury diminish, as evidenced by the decreased demarcation current, and the region at the cross-section develops excitation to some extent. The negative deflection is now less, as the influence of the second phase of the action current becomes evident.

When the interval between preparation and experiment is lengthened, the action current frequently shows itself as a positive variation. In cases where this occurs the demarcation current has subsided to a large extent. The nerve, however, in the neighbourhood of the cross-section is still in an altered condition, and I think we may look upon the positive variation as evidence that the response to the induction shocks is here slower than in the remainder of the nerve, and therefore exercises a greater influence upon the galvanometer.

This is in agreement with the explanation put forward by Waller in so far as that observer distinguished by experiment between this positive variation and fixed anelectrotonus. Waller points out that the variation is particularly sensitive to the action of drugs, differing in that respect from exclusively physical electrotonus.

He contrasts the positive deflection with the usual negative deflection as regards its increase with increasing strength of stimulation. The negative deflection exhibits staircase ascent with a stimulus that is increasing step by step, while the reverse is true of the positive variation, which diminishes as the stimulus is increased, and may ultimately give place to a positive variation.

Waller does not commit himself on the question as to whether or not the appearance of positive or negative action current may depend upon different rates of development of the two states, and considers that the positive variation must be admitted to rank as a true action current, but on the whole he inclines to the view that positive deflection and positive after-deflection are of the same genus and to be interpreted as the sign of a physiologico-chemical assimilation consequent upon previous dissimulation.

This is not in accordance with the view put forward in this paper.

Waller's results have been submitted to criticism by Gotch.* This observer, who used the capillary electrometer, did not find positive change as the initial effect of stimulation in any of his experiments, and is of opinion that Waller's results are all effects due to the development of relative negativity of the tissue under the distal contact. Gotch points out that the method used by Waller, unless extended to comprise rheotome

* Schäfer's Text-book of Physiology, vol. ii., p. 540.

observations, is incapable of giving precise information as to the seat of the changes producing the positive effects.

As mentioned above my experiments with the string galvanometer support Waller's findings. The initial change may appear as a positive deflection, but I agree with Gotch in so far as the initial deflection is concerned, that its cause is relative predominance of occurrences at the distal contact, not indeed because of greater activity here but on account of the slower development of the changes.

If it is true that the positive variation depends for its appearance on difference in time relations between the changes under the two electrodes, we would expect that conditions which slow the processes would suffice to convert a negative into a positive deflection, and this is, as a matter of fact, the case.

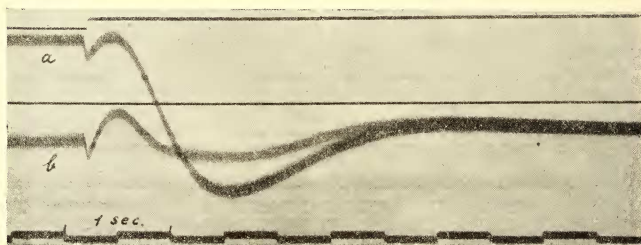


FIG. 3.

Superposed curves obtained from nerves shortly after preparation. Curve *a* at room temperature, Curve *b* after the cross-section has been cooled with cold Ringer's solution. The action current has been changed by cooling from a negative to a positive deflection. The curves show both phases of the positive after-variation and the persisting positive change.

Fig. 3 represents two records obtained from nerves which had been kept in Ringer's solution for two hours after preparation.

The curves are superposed with the zero lines coincident. Curve *a* shows the usual negative deflection during stimulation followed by the after-variation. Curve *b* gives the response obtained after the cross-section had been cooled by cold Ringer's solution. The deflection during stimulation is now positive.

This result justifies us in applying the method of explanation put forward for uninjured nerve, also to the case where the current is led off from longitudinal surface and cross-section, and where the demarcation current has diminished in amount through lapse of time.

So far we have been chiefly considering the initial variation. With regard to the after-variation most observers have followed Hering in attributing it to a process occurring in the uninjured portion of the nerve and affecting the electrode in contact with the longitudinal surface. Strong support has been afforded to that view by Garten's* work.

Gotch takes the view that positive after-variation, when it occurs, is usually due to the presence of a tail or wake of the change under the distal electrode, which is permitted to affect the instrument by some circumstance which diminishes the capacity of the tissue under the proximal contact. He mentions, however, that under other conditions positive after-effects may be developed as appears from the experiments of Hering and Head. As regards the cause and seat of such after-effects Gotch offers no opinion, and his criticism of Waller's conclusions refers only to the initial change.

Cremer,† writing before the publication of Garten's observations, declared that it was not possible upon the evidence so far adduced to decide whether the positive after-effect is due to the proximal electrode becoming more positive or to the distal electrode becoming more negative. He was of opinion that the positive effect only appears when the demarcation current is no longer of its full normal value and waves of negativity can force their way to the second electrode. Further, even conceding that the positive after-effects are conditioned solely by changes at the proximal electrode, it does not follow that the process is opposed to that which gives rise to negative change. There is the possibility that a negative change may persist corresponding to the tonic contraction of muscles, and that a temporary interruption of this may produce the positive after-effect.

With regard to this view of Cremer's, I would point out that I have obtained large positive after-effects from nerves immediately after removal from the body, when the demarcation current produced by the cross-section must be at its height.

The typical persisting effect which I have obtained after tetanisation is positive, while we would expect on Cremer's theory that it should, after a short positive deflection, be negative.

If fig. 1 is referred to it will be observed that the after-effect consists of a fall and rise of the curve, that is to say a positive variation, lasting for 4 to 5 sec., and after this the curve runs parallel to and below the zero line. The interruption of the curve is due to the introduction of a control deflection. It may be many minutes before the zero is regained.

In curve *a* of fig. 3 the after-effect is diphasic, a positive variation being followed by a negative, and the diphasic variation lasts for about 5 sec.

* *Loc. cit.*

† Nagel's Handbuch, Bd. 4, H. 2, s. 903.

There seems little doubt that these after-effects are due to a process occurring in the nerve subsequent to the process which gives rise to the action current. The positive deflection is the first phase, which affects the proximal electrode, and is alone apparent on the curve from nerves where the demarcation current is of its full value. The negative deflection constitutes the second phase and is to be attributed to the distal electrode. The whole deflection is brief, and has run its course in about 5 sec.

Although in the fresh nerve a positive after-effect only is apparent, we cannot exclude the possibility that the process underlying the after-effect

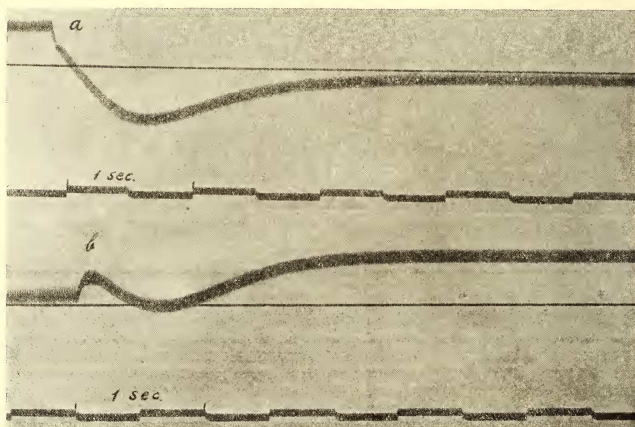


FIG. 4.

Responses from nerves 20 hours after preparation, without fresh section, 2 cm. between leading off electrodes. Curve *a* before cooling, Curve *b* after distal electrode has been cooled.

occurs to some if only a small extent in the neighbourhood of the cross section, and that in such a record as that represented by fig. 1 the curve gives the algebraic sum of the two phases.

In Garten's paper * curves are published (Plate XIX., figs. 2 and 4) from nerves which, at room temperature, showed well-developed positive after-effect, and which after cooling yielded records where this has disappeared, and, as Garten states, the curve returns to its zero position. As a matter of fact, however, careful examination of these curves demonstrates that a small negative after-effect of short duration is present. This may be the

* *Loc. cit.*

sign of a wake of the change under the distal electrode in Gotch's sense, coming to light when the process giving the after-effect is suppressed by cold, or it may be due to after-effect at the distal electrode. Some results that I have obtained seem to indicate that cooling the distal electrode favours negative after-effect. Fig. 4 is an example of this. Curve *a* is taken from a preparation which had been preserved for some hours in Ringer's solution and no fresh section made. Curve *b* was recorded after cooling the tissue under the distal electrode.

In some records taken from nerves at a considerable interval after preparation the negative phase of the after-effect is predominant, so that the curve shows practically only upward deflection at the close of stimulation and the zero line is regained in about 4 sec. This is so in fig. 5, recorded after 20 hours' preservation in Ringer's solution. Here both phases are

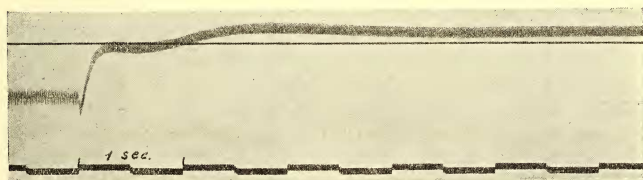


FIG. 5.

Response from nerves 20 hours after preparation, without fresh section. The action current is positive, and the second phase of the after-variation is predominant.

doubtless present, but for some reason the second predominates, and it is of importance to observe that its duration is similar to that of the first phase when alone evident, and of the whole after-variation when both phases are apparent on the curve. This figure gives a response of the type described by Waller as the fifth member of his series, and with regard to which he states that "it was far less frequently and assuredly observed, and I do not know whether in order of development it should be placed before or after the response positive followed by positive."

It appears to me that we are able to distinguish two elements in the electrical changes which follow excitation, one of which is associated with the brief process which occurs in the part or parts of the nerve that have previously been in the condition of excitation, and is evidenced by one or both phases of the positive after variation, and another which shows itself as a persisting positive change, lasting for several minutes after the first short-lived process has terminated. This second intimately depends on the presence and amount of the demarcation current. In the case of fresh

nerves, where the demarcation current is large as in fig. 1, the persisting change has a value of about 5×10^{-5} volt, while the first element gives a change of about 8×10^{-5} volt. When the demarcation current has disappeared the second element is no longer perceptible. It would appear that tetanisation increases the demarcation current when the latter is present.

It is evident that another view of this persisting change might be adopted, and the positive after-variation described as large at first and leaving behind it a wake of less amount and longer duration. The disappearance of the persisting change would then be correlated less with diminution of the demarcation current than with the accompanying development of the second phase and its wake.

We may exclude the possibility that the persisting positive change is caused by *Anelectrotonus*, which depends on the electrolytic polarisability of nerve. The tetanising current used is a weak one, being of minimal or slightly above the minimal strength required to stimulate the nerve.

CONCLUSIONS.

The action current recorded from fresh isolated nerve on tetanisation when the leading off electrodes are placed on longitudinal surface and cross-section is monophasic, or if diphasic, the second phase is very slightly developed. The individual responses to the tetanic shocks are superposed on the deflection.

When the demarcation current has diminished in value the action current is diphasic. Either phase may predominate in the record, depending on two factors—electromotive force and rate of change at the two electrodes.

The after-effect is compounded of two parts: (1) a variation opposite in direction to the action current and monophasic or diphasic according to the condition of the tissue under the distal electrode, and (2) a persisting positive variation, probably to be ascribed to increase in the demarcation current caused by tetanisation.